UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/394,006	09/10/99	BERGER	D P-4762

HM22/0322

RICHARD J RODRICK ESQ
BECTON DICKINSON AND COMPANY
1 BECTON DRIVE
FRANKLIN LAKES NJ 07417

EXAMINER	
FORMAN, B	
ART UNIT	**PAPER NUMBER**
1655	13

DATE MAILED: 03/22/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/394,006	BERGER ET AL.	
	Examiner	Art Unit	
	BJ Forman	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6 .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 16 February 2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/394,006 is acceptable and a CPA has been established. An action on the CPA follows.

The amendments filed 26 December 2000 in Paper No. 9 in which Claim 1 was amended and claims 5, 9 and 11 were canceled is acknowledged. The amendments have been entered. The previous rejections in the Office Action of Paper No.7, dated 21 August 2000 under 35 U.S.C. 112, first paragraph: New Matter are withdrawn in view of the amendments. The previous rejections under 35 U.S.C. 102 (b) and 35 U.S.C. 103 are withdrawn in view of the amendments. The arguments have been thoroughly reviewed, but are deemed moot in view of the amendments and withdrawn rejections. New grounds for rejection are discussed.

Applicant is reminded that changes to 37 C.F.R. § 1.121 require applicant to submit a clean set of all pending claims in addition to the marked up version of the amended claims.

Currently claims 1-17 are under prosecution.

Specification

2. The spacing of the lines of the specification is such as to make reading and entry of amendments difficult. New application papers with lines double spaced on good quality paper are required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

First paragraph of 35 U.S.C. 112: New Matter

4. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims as amended are drawn to compositions for stabilizing the structure and nucleic acids of at least one cell said composition comprises of a first substance capable of precipitating or denaturing proteins whose concentration is less than 80% of the total composition and a second facilitator substance to aid in the infusion of the first substance whose concentration is greater than 20% of the total composition wherein the combined concentration of said first and second substances is 100% of the composition. The claimed compositions encompass a very large genus of compositions comprising composition concentrations not disclosed in the specification i.e. a first substance having a large genus of concentrations ranging from 0.001% to 79.99% and a second substance having a large genus of concentrations ranging from 20.001% to 99.99%. The specification teaches the preferred embodiment is 50% metnaol/50% DMSO (page 4, lines 19-24). Additionally, the specification teaches 80% methanol/20% DMSO; 50% methanol/50% DMSO; and 100% methanol; 40% methanol + 40% ethanol/ 20% DMSO; 25% methanol + 25% ethanol/ 50% DMSO; and 80% ethanol/20%DMSO; 20% methanol/80% DMSO; 40% methanol/60% DMSO; 60% methanol/40% DMSO; 100% methanol; and 100%DMSO (Examples 4-12, pages 14-19, 21 & 23). However, the specification does not teach the very large genus of claimed compositions i.e. a first substance having concentrations ranging from 0.001% to 79.99% and the second substance having concentrations ranging from 20.001% to 99.99% (e.g. 78% alcohol/ 22% DMSO). Therefore the claims, as amended, introduce new matter not disclosed in the

specification as originally filed. It is suggested that the claims be amended to claim the invention as recited in the specification as originally filed.

First paragraph of 35 U.S.C. 112: Written Description

5. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims, as amended, are drawn to a composition for stabilizing the structure and nucleic acids of at least one cell. The specification teaches the claimed composition stabilizes vaginal swab samples (page 7, lines 7-9 and 24-26). Additionally, the specification teaches specific cell types found in vaginal fluid i.e. *Trichomonas vaginalis*, *Gardnerella vaginalis* and *Candida albican* and the claimed compositions' stabilization of the structure and nucleic acids in these cell types (pages 11-12, Examples 2 & 4-12). The specification suggests the composition "could be used for other biological specimens" (page 4, lines 26-29). However, the specification does not teach the composition stabilizes the structure and nucleic acids of other specimens in the very large genus of cells as claimed. The claimed cell encompasses eukaryotic cells which further encompasses plant and animal cells each of which further encompass numerous species and sub-species, prokaryotic cells which further encompasses bacteria which further encompasses numerous species not described in the specification. The specification fails to teach a representative number of the claimed species. The specification teaches various formulations of the claimed composition and experimental conditions using the compositions (Examples 4-12) but the specification does not teach using the claimed composition with a representative number of the claimed cell species. Therefore, the specification does not provide a written description of the claimed composition in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The

courts have stated that the specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonable conclude the inventor had possession of the claimed invention see *In re Vas-Cath*, Inc. 935F2d. 1555, 1563, 19 USPQ2d 1111,1116. It is suggested that the claims be amended to claims the invention as described in the specification e.g. by inserting "in vaginal fluid" after "one cell" in line 2 of Claim 1.

Response to Arguments

6. Applicant argues that the present invention does not have to be limited to cells in the vaginal fluids because Example 13 of the specification teaches that cells other than just microbial cells can be "stabilized". This argument is not found persuasive because the cells "stabilized" in Example 13 were subjected to only one of the many claimed compositions (i.e. 1:1 methanol : DMSO) and two of the cell types "stabilized" in Example 13 are found in vaginal fluid. Additionally, the cells of Example 13 were only analyzed visually for cell lysis (page 24, lines 13-16) and were not analyzed for stabilized cell structure and nucleic acids as claimed.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-4, 6-8, 10, & 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gee et al. (U.S. Patent No. 6,162,931, filed 12 April 1996), Williams et al. (Journal of Clinical Microbiology, 1995, 33(6): 1558-1561), Connelly et al. (U.S. Patent No. 5,422,277, filed 27 March 1992) Tometsko (U.S. Patent No. 5,229,265, filed 13 March 1990), Evinger-Hodges et al. (WO 90/02204, published 8 March 1990) and Bresser et al. (U.S. Patent No. 5,521,061, filed 17 July 1992).

Regarding Claim 1, Gee et al. teach a composition for stabilizing the structure and nucleic acids of at least one cell in a sample (i.e. fix and permeabilize, Column 30, lines 54-56) comprising; a first substance capable of precipitating or denaturing proteins comprising alcohol i.e. a fixative solution comprising methanol, and a second facilitator substance to aid in the infusion of the first substance into said at least one cell i.e. DMSO, wherein the concentrations of said first and second substances are effective to stabilize the structure and nucleic acids of said at least one cell (Column 30, lines 46-60); wherein the methanol stabilizes cell by fixation and the DMSO permeabilizes the cell to facilitate infusion into the cell (Column 30, lines 49-60) but they do not teach the concentrations of the first and second substance wherein the combined concentrations is 100% of the composition. However, as noted by Gee et al. (Column 30, lines 46-51), the prior art is replete with compositions for fixing cells so as to preserve cellular morphology by stabilizing cell structure and nucleic acids and to permeabilize so as to facilitate transport across the cell membranes wherein the concentrations of the components of the compositions vary greatly relative to cell type and desired results. For example, Williams et al. teach a composition for stabilizing the structure and nucleic acids of a cell (i.e. bacterial cells) comprising at least one alcohol (i.e. ethanol) which is effective for precipitating or denaturing proteins wherein the concentration is less than 80% (i.e. 50, 70%, 75%) of the total composition (page 1558, right column, third full paragraph); Connelly et al. teach a composition for stabilizing the structure and nucleic acids of a cell (i.e. prokaryotic and eukaryotic cells (Column 9, lines 20-22) comprising a facilitator substance i.e. DMSO whose concentration is greater than 20% i.e. about 20% (Column 7, line 61-Column 8, line 2); Tometsko teaches a composition for stabilizing the structure and nucleic acids of a cell (red blood cells) comprising at least one alcohol i.e. methanol (Column 7, lines 5-29) wherein the method further comprises a second facilitator substance i.e. DMSO (Column 6, lines 66-68); Evinger-Hodges et al. teach a composition for stabilizing the structure and nucleic acids of a cell i.e. optimal fixation (page 4, lines 22) the composition comprising an alcohol and a

facilitator substance i.e. 50% methanol/50% acetone (page 13, lines 24-35) wherein Gee et al. teach acetone is a facilitator effective for aiding infusion (Column 30, lines 54-56); and Bresser et al. teach a composition for stabilizing the structure and nucleic acids of a cell comprising at least one alcohol and a second facilitator substance i.e. DMSO wherein the concentrations of the components are variable (Column 2, lines 19-33). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply teachings generally known within the art to modify the fixative solution of Gee et al. and by routine experimentation with a specific cell-type alter the composition components and component concentrations to thereby optimize experimental conditions and maximize experimental results for the specific cell-type. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 2, Gee et al. teach the composition wherein the alcohol is methanol (Column 30, lines 46-49).

Regarding Claim 3, Gee et al. teach the composition wherein the second substance is dimethyl sulfoxide (DMSO) (Column 30, lines 54-56).

Regarding Claim 4, Gee et al. teach the composition wherein the first substance is comprised of one alcohol (Column 30, lines 46-49).

Regarding Claim 6, Gee et al. teach the composition wherein the first substance is comprised of one alcohol (Column 30, lines 46-49) but they do not teach the first substance is comprised of a first alcohol or ketone and a second alcohol or ketone. However, Tometsko teaches the similar composition wherein the first substance comprises a first alcohol and a second ketone i.e. methanol/acetone (Column 7, lines 27-29). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the first substance comprising one alcohol as taught by Gee et al. to further comprise a second ketone

as taught by Tometsko based on cell type being stabilized for the obvious benefit of optimizing stabilization for the specific cell type and to thereby maximize experimental results.

Regarding Claim 7, Gee et al. do not teach the first substance is comprised of a first alcohol or ketone and a second alcohol or ketone. However, Tometsko teaches the similar composition wherein the first substance comprises a first alcohol and a second ketone i.e. methanol/acetone (Column 7, lines 27-29) but they do not teach a ratio for the components of the composition. However, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the first substance comprising one alcohol as taught by Gee et al. to further comprise a second ketone as taught by Tometsko and using routine experimentation to optimize the ratio of components in the composition for each specific cell type being stabilized for the obvious benefit of optimizing stabilization for the specific cell-type to thereby maximize experimental results.

Regarding Claim 8, Gee et al. teach the composition comprises a first substance and a second substance (Column 30, lines 46-56) but they do not teach the ratio or the components in the composition. However, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the ratio of the components in the composition taught by Gee et al. using routine experimentation optimize the ratio of component in the composition for each specific cell type to be stabilized for the obvious benefit of optimizing stabilization for the specific cell-type to thereby maximize experimental results.

Regarding Claim 10, Gee et al. teach the composition wherein said first substance is methanol and said second substance is DMSO (Column 30, lines 46-56) but they do not teach the composition wherein the first substance comprises a first alcohol and a second alcohol or ketone. However, Tometsko teaches the similar composition wherein the first substance comprises a first alcohol and a second ketone i.e. methanol/acetone (Column 7, lines 27-29) but they do not teach a ratio for the components of the composition. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify

the first substance comprising one alcohol as taught by Gee et al. to further comprise a second ketone as taught by Tometsko based on cell type being stabilized for the obvious benefit of cell type-specific optimization of stabilization.

Regarding Claim 12, Gee et al. teach the composition wherein said first substance is methanol and said second substance is DMSO (Column 30, lines 46-56).

Regarding Claims 13-15, Gee et al. teach the composition wherein RNA is stabilized (Example 127). Additionally, Evinger-Hodges et al. teach the composition wherein DNA (Claim 13), RNA (Claim 14) and ribosomal RNA (Claim 15) is stabilized (page 6, lines 1-7). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made that to apply the methanol fixative of RNA as taught by Gee et al. to a composition of for fixing DNA, RNA and ribosomal RNA as taught by Evinger-Hodges et al. for the obvious benefit of stabilizing total cellular nucleic acids and for the expected benefit of detecting multiple nucleic acids simultaneously as taught by Evinger-Hodges et al. (page 3, lines 29-31).

Regarding Claim 16, Gee et al. teach the composition wherein said at least one cell is a prokaryote i.e. bacterium (Column 30, lines 17-20).

Regarding Claim 17, Gee et al. teach the composition wherein said at least one cell is a microorganism i.e. bacterium or virus (Column 30, lines 17-20).

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
March 20, 2001

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

3/21/a